How FDA Promotes Partnerships to Accelerate Medical Product Development

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How does FDA encourage broad stakeholder efforts to generate drug development tools?

How does FDA respond to a rapidly changing scientific landscape? How does FDA incorporate the patient's voice?

How can FDA collaborate with other regulatory agencies toward greater concurrence in regulatory requirements in areas of unmet medical need?

What are the benefits of such collaborations, especially between the US and EU?

How does FDA measure success?

General Agreement: Development of Evaluative Tools-- A Tremendously Neglected Area

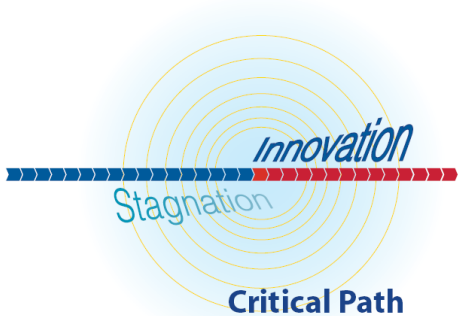
- Now: “Build an airplane and then see if it can fly”
- Better science is needed to both predict and assess safety and efficacy of investigational products
- Major causes of failure in Phase 3 clinical development
  - Lack of effectiveness against placebo or active control
  - Unexpected drug toxicity
  - Commercial non-viability (not better than existing therapy)

Need for Evaluative Tools

- Large amount of biochemical/molecular knowledge but few ways to assess state of whole organism and impact of interventions at the organism level
- Most assessment tools are not standardized so limited ability to compare one experiment to another
- Little insight into sources of variability of treatment response, even current therapies
- As a result, most clinical development programs are “brute force” empirical efforts: extremely costly and time-consuming

Critical Path Opportunities List

U.S. Department of Health and Human Services
Food and Drug Administration



Critical Path Opportunities Report

U.S. Department of Health and Human Services
Food and Drug Administration
March 2006

July | 11

Identifying CDER's Science and Research Needs Report

July 2011

The CDER Science Prioritization and Review Committee (SPaRC)

Center for Drug Evaluation and Research

Predicting, Measuring, and Improving Efficacy Needs:

- New endpoints
- New trial designs
- Use of biomarkers to subset disease (prognostic or response predictors)
- Use of patient-reported outcomes
- Conducting natural history studies to understand disease course—particularly in rare diseases

What is CDER doing to catalyze movement from concept to action?

Examples of Collaborative Efforts

- Cardiovascular Safety Research Consortium
- Serious Adverse Events Consortium
- Biomarkers Consortium
- Clinical Trials Transformation Initiative
- Critical Path Institute
  - Predictive Safety Testing Consortium (PSTC)
  - Patient Reported Outcomes (PRO) Consortium
  - Coalition Against Major Diseases Consortium
  - Critical Path to TB Drug Regimens
  - Polycystic Kidney Disease (PKD) Consortium
  - Multiple Sclerosis Outcome Assessments Consortium
  - ePRO Consortium
  - Coalition for Accelerating Standards and Therapies (CFAST)
- Analgesic Clinical Trials Translation, Innovation, Opportunities and Networks (ACTTION) Initiative

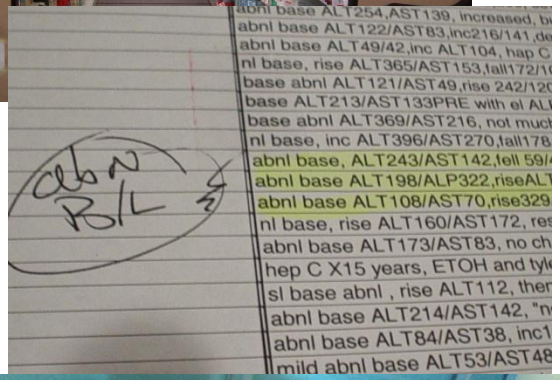
Drug Development Tool (DDT) Qualification Activities

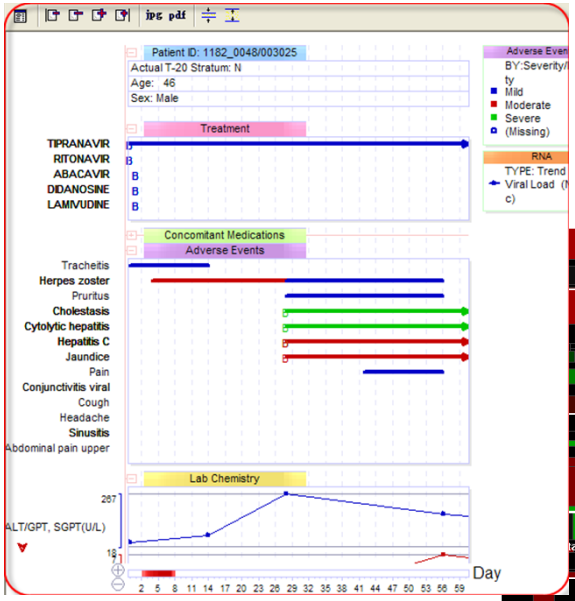
www.fda.gov/Drugs/DevelopmentApprovalProcess/DrugDevelopmentToolsQualificationProgram/default.htm

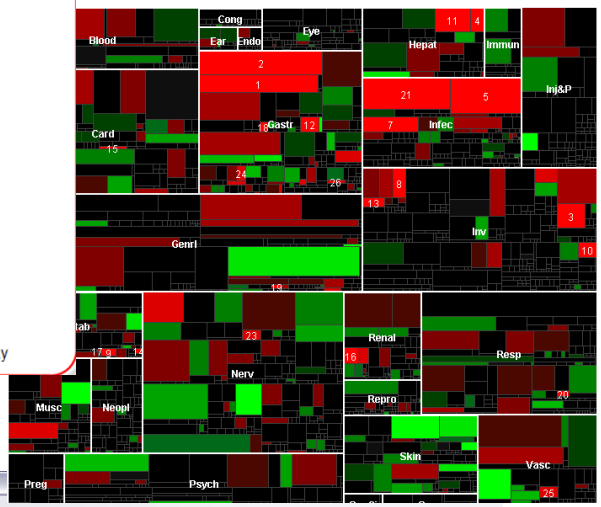
Innovative Clinical Trial Designs Guidance Development

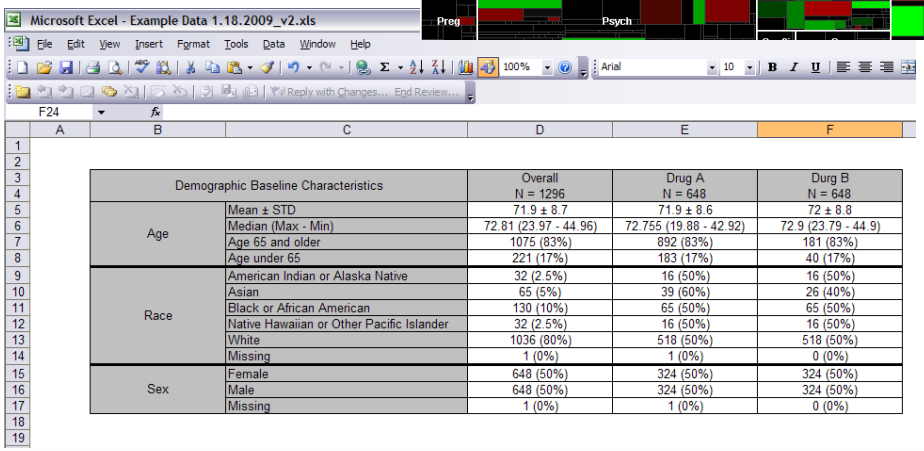
- Advancing Innovative Trial Designs
  - Adaptive Trial Designs (draft published)
  - Non-inferiority Trial Designs (draft published)
  - Multiple Endpoint Analysis (in development)
  - Enrichment Designs (draft published)
  - Treatment of Missing Data (in development)
- Additional Topics
  - Meta-Analysis Approaches for Efficacy and Safety Data
    - (in development)
  - Qualification Process for Drug Development Tools
    - (draft published)

Data Submissions









Demographic Baseline Characteristics		Overall N = 1296	Drug A N = 648	Durg B N = 648
Age	Mean ± STD	71.9 ± 8.7	71.9 ± 8.6	72 ± 8.8
	Median (Max - Min)	72.81 (23.97 - 44.96)	72.755 (19.88 - 42.92)	72.9 (23.79 - 44.9)
	Age 65 and older	1075 (83%)	892 (83%)	181 (83%)
	Age under 65	221 (17%)	183 (17%)	40 (17%)
Race	American Indian or Alaska Native	32 (2.5%)	16 (50%)	16 (50%)
	Asian	65 (5%)	39 (60%)	26 (40%)
	Black or African American	130 (10%)	65 (50%)	65 (50%)
	Native Hawaiian or Other Pacific Islander	32 (2.5%)	16 (50%)	16 (50%)
	White	1036 (80%)	518 (50%)	518 (50%)
	Missing	1 (0%)	1 (0%)	0 (0%)
Sex	Female	648 (50%)	324 (50%)	324 (50%)
	Male	648 (50%)	324 (50%)	324 (50%)
	Missing	1 (0%)	1 (0%)	0 (0%)

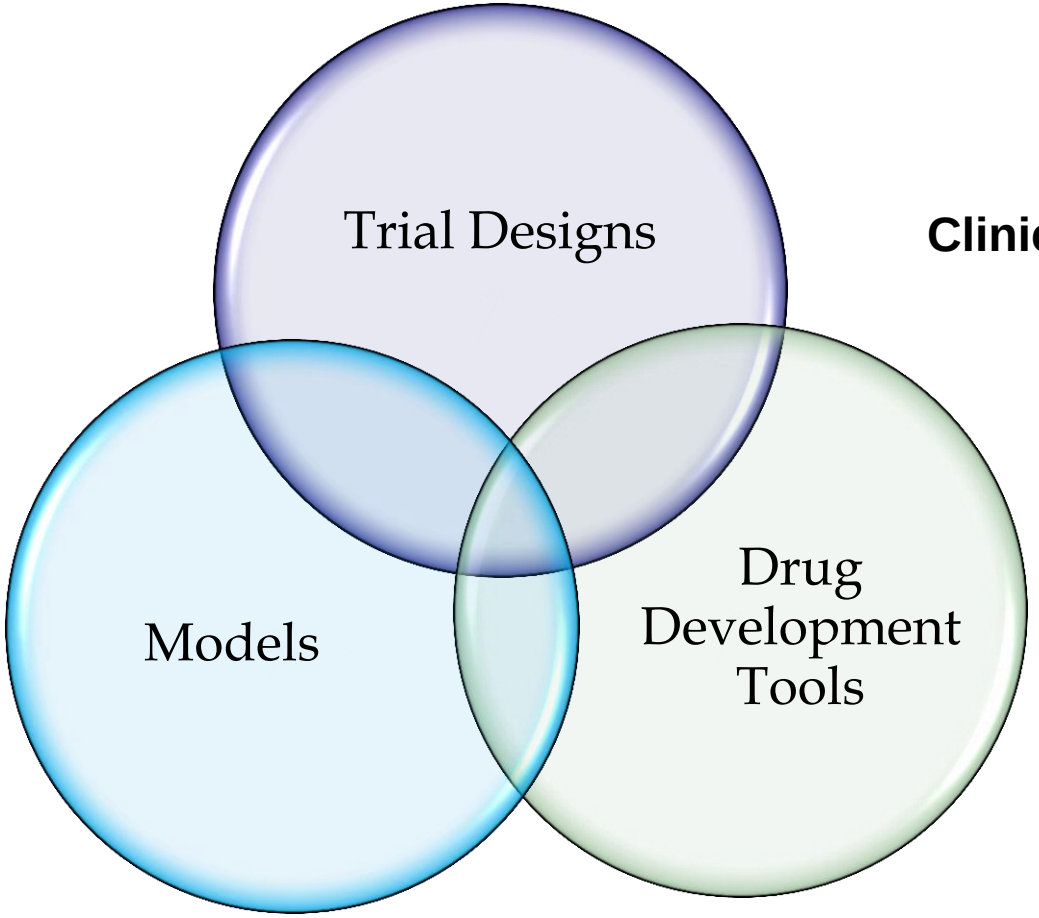
Creating an Integrated Workforce--Training

- Clinical Investigation
- Drug Development
- Regulatory Science
- Medical Informatics/Computational Science
- Statistics

- Concept: Creation of integrated training hubs for online/deployable content and training for international investigators, regulators, etc.

Current Areas of Activity

Data Standards



Clinical Trial Networks

Training

Data Sharing

How Can We Collaborate with Other Regulatory Agencies More Effectively?

- Data Sharing
  - CPath-IMI-Biomarkers Consortium—renal biomarkers
- Cooperation re: Data Sharing
  - Share plans and coordinate activities between international partners)
- Share Best Practices
- Coordinate data requests for DDT Qualification submissions
- Share Discussion of Key Initiatives/Activities and Outcomes
  - Joint liaisons to key initiatives
  - PSTC and SAFE-T Consortium
- Remove Redundancy--Proactive sharing of strategy and plans
- Build Collaborative IT Platforms

How do we measure success?

- Approvals of new medical therapies
- Development of new guidance
- Integration of novel biomarkers into regulatory review processes
- Proactive sharing of pre-competitive data
- Development of data warehouses based on standardized data in order to leverage prior knowledge
- Streamlined coordination of information among international regulators

CDER'S 2012 NMEs

39 novel new drugs in CY 2012:
In Calendar Year 2012, FDA's Center for Drug Evaluation and Research (CDER) approved 39 novel new medicines, known as new molecular entities (NMEs).* This includes applications for both New Drug Applications (NDAs) and Biologics License Applications (BLAs).

The blue bars in the chart to the right indicate the number of NMEs approved by CDER in each year of the past decade. CDER approved 39 NMEs in 2012, the highest total for this period. From 2003 through 2011 CDER has averaged about 24 NME approvals per year. The 2012 total is 63% higher than this previous nine year average.

In 2012 CDER approved 39 NME's

FDA is encouraged by this increase; however, it is too early to tell if it reflects a long-term trend toward increasing numbers of product approvals.

Applications for new approvals remain steady
Despite a higher number of NME approvals for the past two years, the number of applications CDER has been receiving for NMEs has not been consistently and significantly increasing.

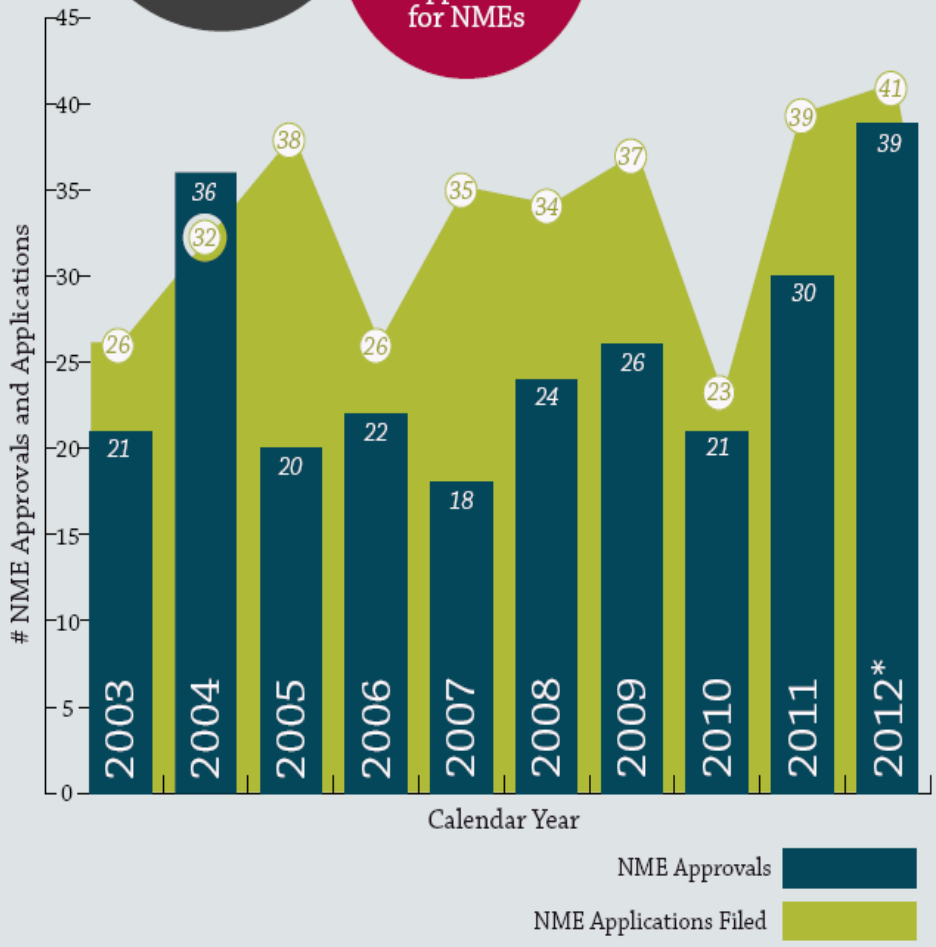
The green portion of th graph to the right indicate the number of new NDA and BLA applications for NMEs CDER has filed over the last ten years. From 2003 through 2011, CDER filed an average of about 32 applications for NMEs per year. Although all applications submitted in 2012 were not accepted for filing as of 12/31/12, CDER projects about 41 for 2012, roughly 28% higher than the 2003-2011 average of 32.

Forty-one filings of new NME applications in CY 2012 would be the most this decade, another positive sign. However, the recent increase in NME filings is not enough to predict a trend toward sustained growth. FDA cannot expect a continuing upward trend for NME approvals until a sustained increase in the number of applications for NMEs submitted for approval is also demonstrated.

The NMEs of 2012: see pages 14 & 15 for what these drugs are used for.							
Amyvid	Aubagio	Belviq	Bosulif	choline C-11	Cometriq	Elelyso	Eliquis
Erivedge	Fulyzaq	Fycompa	Gattex	Iclusig	Inlyta	Jetrea	Juxtapid
Kalydeco	Kyprolis	Linzess	Myrbetriq	Neutroval	Omontys	Perjeta	Picato
Prepopik	raxibacumab	Signifor	Sirturo	Stendra	Stivarga	Stribild	Surfaxin
Synribo	Tudorza Pressair	Voraxaze	Xeljanz	Xtandi	Zaltrap	Zioptan	

39 NMEs approved in CY 2012 is the highest total approved by CDER in more than a decade

From 2003 through 2011 CDER filed an average of about 32 applications for NMEs



*The final number of NME Applications filed in 2012 is projected, pending final validation of the data and dependent on the outcome of applications submitted in late 2012.

Impact on Public Health

Notable NMEs of 2012: An exceptional year for quality

In addition to the noteworthy examples of innovative First-in-Class and "Orphan" new products mentioned on page 4 and highlighted on these pages, the 39 NMEs approved in CY 2012 also include the following notable new products: Elelyso, for Gaucher disease, Eliquis, an anticoagulant to help prevent a type of blood clot known as a venous thromboembolism, Jetrea, to treat an eye condition called symptomatic vitreomacular adhesion, raxibacumab, to treat inhalational anthrax, and Stribild, a once-a-day combination pill to treat HIV-1 infection in adults who have never been treated for HIV infection.

Amyvid: to help rule out Alzheimer's disease as a cause of mental decline

Gattex: to treat short bowel syndrome

Juxtapid: to treat homozygous hypercholestertolemia

Voraxaze: to help avoid toxic effects of methotrexate

Kalydeco: to treat cystic fibrosis

Signifor: to treat Cushing's disease

Sirturo: to treat multi-drug-resistant pulmonary tuberculosis

Bosulif, Iclusig, & Synribo: to treat chronic myelogenous leukemia

Fulyzaq: to treat HIV-associated diarrhea

Erivedge: to treat late-stage basal cell cancer

Other notable NME approvals of CY 2012 include innovative drugs to treat a variety of cancers, such as, Perjeta, to treat a specific form of late-stage breast cancer, Stivarga, to treat patients with colorectal cancer that has progressed after treatment and spread to other parts of the body and Xtandi for late-stage prostate cancer.

Proposal

- Create collaborative platforms which provide a global mapping of Public Private Partnership (PPP) activities
  - Internal—Allows an interface for PPPs to collaborate and share information safely
  - External—Allows potential stakeholders to identify efforts to support
- Benefits—Allow PPPs to identify current efforts for collaboration internationally and target gaps for future development